



410.018

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:  
MICHAEL ARAND et al  
Serial No.: 10/009,030  
Filed: November 2, 2001  
For: EPOXIDE...ORIGIN

:  
: Examiner: C. Patterson  
:  
: Art Unit: 1652  
:  
475 Park Avenue South  
New York, NY 10016

**DECLARATION**

Hon. Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Roland Furstoss hereby deposes and says:

That he received his doctorate in Organic Chemistry from Strasbourg, France in 1967 and D. Sc. in Organic Chemistry from Marseille, France in 1972.

That he had a Post-doctoral stay at Ohio State University from 1972-1973.

That he has been working in the field of Biocatalysts applied to fine organic synthesis for more than 25 years with a focus on (1) hydroxylation of unactivated carbon atoms, (2) epoxidation and dihydroxylation of olefinic double bonds, (3) Baeyer-Villiger oxidations and (4) epoxide hydrolases catalyzed hydrolytic kinetic resolutions.

That -to date- he is the author or co-author of 128 publications, 132 communications and has given 83 invited lectures.

That he is a coinventor of the above application.

That to the best of his knowledge, the epoxide hydrolase claimed in the above application was the first epoxide hydrolase of fungal origin ever purified and studied.

That the Nellaiah et al and Morisseau et al publications cited by the Examiner in the above application both relate to the use of an epoxide hydrolase preparation from *Aspergillus niger* but not a purified epoxide hydrolase.

That the Nellaiah reference relates to the enantioselective hydrolysis of p-nitrostyrene oxide by an epoxide hydrolase preparation from *Aspergillus niger*.

On page 71 of the Nellaiah publication, the preparation corresponds to the high speed supernatant of an *Aspergillus niger* broken cell suspension which is not a purified epoxide hydrolase.

The Morisseau publication only describes a procedure for obtaining enzymatic activity out of whole fungal cells and the preparation described therein is only a very crude cell extract.

That, at the time of applicants' invention and due to the novelty of this "first fungal epoxide hydrolase discovery", it was impossible for one person ordinary skilled in the art to predict any efficient purification method for this enzyme since, at the time of Applicants' invention, no one had any idea about its thermal stability, its stability in the presence of salts, the type of columns to be used, its stability upon the overall purification process and the like.

That this issue was even more uncertain due to the fact that Applicants rapidly suspected this protein to be multimeric, and was later observed to be tetrameric.


That one skilled in the art would not know what its behavior would be and the remaining activity upon purification of such a potentially fragile enzyme multimer really was unpredictable

That Applicants worked very diligently for several months, if not a year, to set up the efficient purification conditions finally described in reference V and, therefore, the said Morisseau et al reference in no way anticipates or renders obvious Applicants' invention.

Moreover, no information was known at the time of this invention about the genetic aspects related to this enzyme. Therefore, no scientific information necessary for overexpression of this enzyme, which later on proved to be rather complicated as described in ref V, could be deduced by one skilled in the art.

That the Chartrain et al patent only mentions an indefinite epoxide hydrolase activity using "suspension of whole fungal cells" of the two fungus strains *Diplodia gossipina* or *Lasiodiplodia theobromae* which has nothing to do with the *Aspergillus* genus claimed in Applicants' application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 USC 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

By:   
Roland Furstoss

Dated: 3/03/05